Time delays in the diagnosis and treatment of malaria in non-endemic countries: A systematic review

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Abstract

Background

Delays in diagnosis and treatment for malaria are associated with an increased risk for severe disease and mortality. Identifying the extent of patient and health system delay can provide a benchmark against which interventions to reduce delays can be measured.

Methods

We performed an electronic search in PubMed, EMBASE, Web of Science and LILACS for studies reporting time to diagnosis and treatment after return from travel, onset of symptoms and seeking healthcare in non-endemic countries. Additionally, theses, conference proceedings and nationally reported surveillance data were also searched for information on time delays. There were no language restrictions and all the studies were assessed for methodological quality.

Results

Data from 69 papers out of 1,719 identified records published between 2005 and 2017 were extracted; our findings show that median diagnosis delays of four or more days are common and patient delays accounted for a large proportion of diagnostic delay. There were limited data available on medical diagnostic delay.

Conclusion

Patient delays accounted for a large proportion of the overall diagnostic delay; however the retrospective nature of the studies could have overestimated patient delay since previous healthcare contacts were not included. Additionally, the high frequency of studies reporting a clinically significant delay is a major concern.

Background

Prompt diagnosis and treatment of malaria remains a challenge in non-endemic countries [1]. Both patient factors and medical factors can lead to delays in diagnosis and treatment. In non-endemic countries specifically, differing immunogenic profiles, chemoprophylaxis use, the small number of cases and the non-specific symptoms associated with malaria add to the challenge of early diagnosis and treatment [1], [2], [3]. Furthermore, it is likely to become more challenging as the number of imported malaria cases decline due to global malaria eradication efforts [4].

Identifying where the greatest delays occur can provide a benchmark against which interventions to reduce delays can be measured. In this review, we describe the duration of delay at different time periods leading up to a diagnosis and treatment of malaria in non-endemic countries. Additionally, we describe the delays by parasite species given the species specific variations in disease manifestation, and the heterogeneity in the composition of plasmodium species types imported to non-endemic countries [5]. Finally, we discuss the implications of how data on delay are collected and reported amongst the included studies on the interpretation of the results of this review.

Methods

Search strategy

The search was carried out in three stages. The first stage involved searching for published academic papers in electronic databases (PubMed, Web of Science, EMBASE and LILACS). The second stage involved searching for unpublished work in grey literature databases. The final stage involved searching for nationally reported malaria surveillance data from non-endemic countries. The search was restricted to studies published from January 2005 to November 2016 to retrieve contemporary data and there were no language restrictions. A detailed search strategy including the search terms used for each stage is summarised in appendix A.1. The systematic review protocol has been registered and published on PROSPERO (Record number: CRD42016045259).

Inclusion criteria

Observational studies including case series, case control and cohort studies which reported on time delays were included. For case control studies specifically, studies were only included if all malaria patients at the study centre were recruited as cases, and if the time delays were reported at baseline. This was done to minimise the effect that selection bias might have on the results of the review.

Studies with participants of all ages diagnosed with malaria in a non-endemic country were included in the review irrespective of whether they focused on a specific ethnicity or traveller group (e.g. those who visit friends and relatives overseas). Studies were grouped by parasite species (i.e. *P. falciparum, P. vivax, P. ovale, and P. malariae*) provided that the majority (greater than 70%) of the participants in the study were attributable to that species. Studies that did not report the parasite species or had less than 70% of cases attributable to a specific parasite species were included in the "mixed" category. Additionally, studies which reported data for severe malaria or children (aged <=18 years) were included and analysed separately. The severe malaria category consisted of studies which reported cases of severe malaria as per the WHO classification, or those who have been admitted to ICU with malaria, or fatal cases of malaria [6].

Studies were included in the review if they recruited >=20 participants, were conducted in a non-endemic country according to the WHO official register and supplementary list (2012) (Appendix A.1) [7], had a study period which ended after the 1st of January 2000 and report on any of the following outcomes (Figure 1):

- Time to onset of symptoms (TOS): This is defined as the time between returning from a malaria endemic country and the onset of symptoms for malaria.
- Diagnostic delay (DD): For this review, diagnostic delay is defined as the time between the onset of symptoms and the diagnosis of malaria.

- Delay in seeking healthcare: This is also known as patient delay (PD) and is defined as the time between the onset of symptoms and first attending a medical facility or seeking healthcare advice.
- Medical diagnostic delay (MDD): This is defined as the time between first attending a medical facility or seeking healthcare advice and the diagnosis of malaria.
- Treatment delay (TD): This is defined as the time between the onset of symptoms and the initiation of treatment for malaria.
- Medical treatment delay (MTD): This is defined as the time between first attending a medical facility or seeking healthcare advice and the initiation of treatment for malaria.

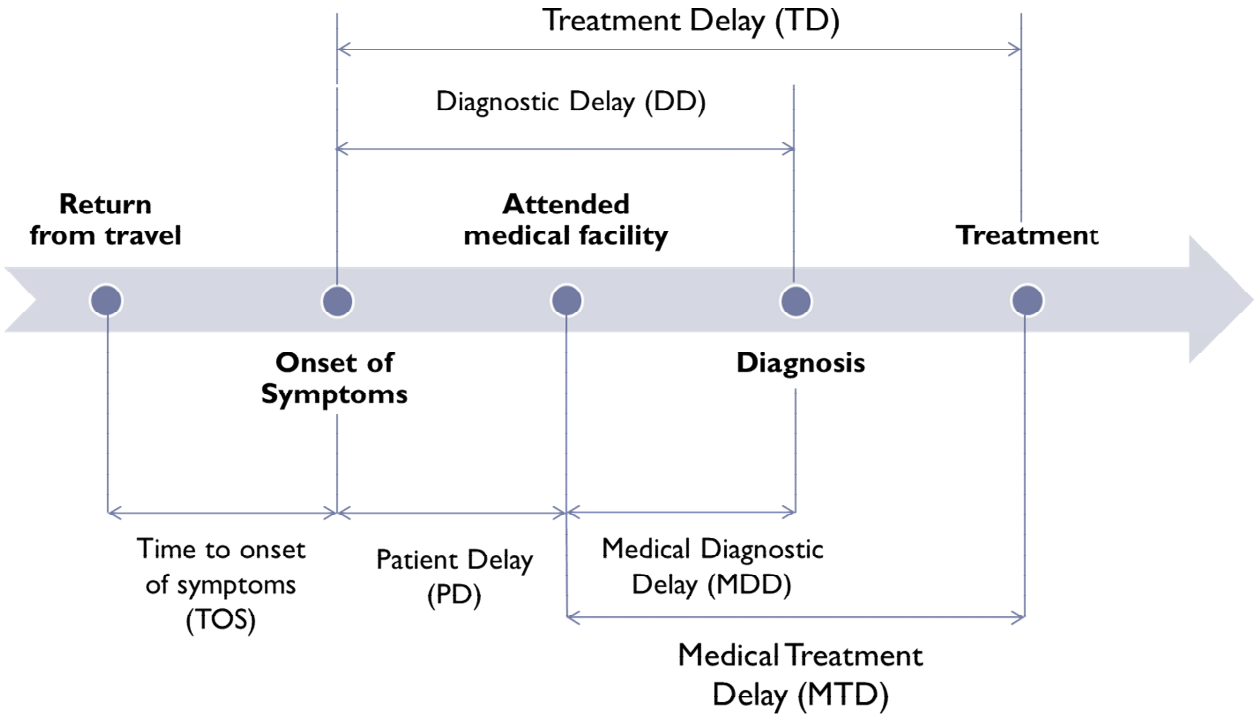

Figure 1. A timeline summarising the definitions of the various time delays included in this review

When more than one study described data from the same source, the study with the more complete data was selected for the review. If the completeness of the data was similar, then the more recent data were selected for the review.

Data collection

The citations of the studies retrieved using the review's search strategy were downloaded, indexed and de-duplicated using Endnote version x7. The title and abstracts were screened independently by two reviewers (HB and JC) to identify studies which potentially met the inclusion criteria. The full text of all potentially relevant articles was obtained and reviewed and the reviewers (HB and JC) independently classified the studies into the following categories: "include", "exclude" or "unclear". Disagreements in the classification of the studies were resolved by consensus or by a third reviewer (GR) if no agreement was reached. A similar approach was used for the studies which were classified as "unclear" to reach a decision on whether to include or exclude the study. The reason for exclusion for all the rejected studies was documented and is summarised in the results (Figure 2).

Data extraction

Data were extracted from the studies selected for inclusion using a standardised data collection form. The data extracted included: study author, study year, study design, country, description of study participants, sample size, proportion of participants with *P. falciparum* infection and the main outcomes (time to the onset of symptoms, diagnostic delay, patient delay, medical diagnostic delay, treatment delay and medical treatment delay). For the main outcomes, data were extracted if either the mean or the median duration of delay was reported, as well as the standard deviation (SD) or interquartile range (IQR).

Both reviewers independently extracted the data and entered it into an Excel spreadsheet. The extracted data in both Excel spreadsheets were checked by HB for inconsistencies and both reviewers (HB and JC) re-reviewed the studies if any were found to ensure the correct data were extracted. If the studies selected for inclusion had relevant unreported data, the study's corresponding author was contacted by email to request the data.

All studies which were included in the review were assessed for methodological quality using the "JBI critical appraisal checklist" (appendix A.2).

Data Synthesis

Extracted data from the studies were summarised in tables to provide a descriptive synthesis of the included studies. The tables were presented separately for each of the time delays (TOS, DD, PD, MDD, TD and MTD). The data in each of the tables were categorised in subgroups according to the plasmodium species (*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae* and mixed species). Studies which specifically reported on children and those with severe malaria were categorised separately within the tables.

For studies which report both the median and the IQR (25^{th} and 75^{th} percentile), the data were summarised in boxplots to allow for comparison of the delays between the included studies. Additionally, for studies which reported median delays, a summary median, IQR and range was provided using boxplots for *P. falciparum* and *P. vivax* only.

Results

Description of studies

Electronic database search

The PubMed search retrieved a total of 1,061 citations. Excluding studies already retrieved from the PubMed search, the WOS, EMBASE and LILACS searches retrieved a further 169, 109 and 32 citations respectively. In total the electronic databases searches retrieved 1,371 citations of which 64 studies met the inclusion criteria.

Grey Literature search

The grey literature search retrieved a total of 253 citations. Of these, 18 were considered for full text review after reviewing the title and abstracts of the theses and conference proceedings. A further 7 were excluded after reviewing the full text. The full text was not available for 11 theses (non-loanable) either online or through interlibrary loans. Therefore there were no studies added to the review as a result of the grey literature search.

National agency reports

Of the 94 countries certified as non-endemic by the WHO, the organization responsible for the surveillance of imported malaria was identified in 85 of them. Publicly available reports on malaria surveillance were identified from 64 of these organisations, however, for the majority of these (N= 60), the reports contained annual summaries on the number of imported malaria cases with no information on time delays. For 3 organisations (France, Tunisia and Le Reunion), information on time delays was available and data from the surveillance summaries reported by these organisations were included in the review. For France, annual surveillance data is published in the "Centre National de Référence sur le Paludisme" (CNRP) website and data on time delays is available for the years 2006 to 2010 [8]. For Tunisia and Le Reunion, information on time delays was available for the years of 2002-2007 and 2003- 2007 respectively. For a further 2 organisations, the Centres for Disease Control and Prevention (United States) and National Institute of Public Health (Poland), annual surveillance summaries reported data on time delays, however no mean or median was reported. The authors of the surveillance reports were contacted and data from these 2 organisations were included in the review [9], [10].

Included studies

There were a total of 69 studies included in the review following the electronic database, grey literature and national agency report searches (Figure 2). In some of these studies, data were

available for a number of species of malaria as well as different time delays resulting in the same study contributing data for a number of different outcomes in this review. A table summarizing the characteristics of the included studies as well as the delays reported in the studies can be seen in (appendix A.5). There were no studies excluded after quality assessment (appendix A.2).

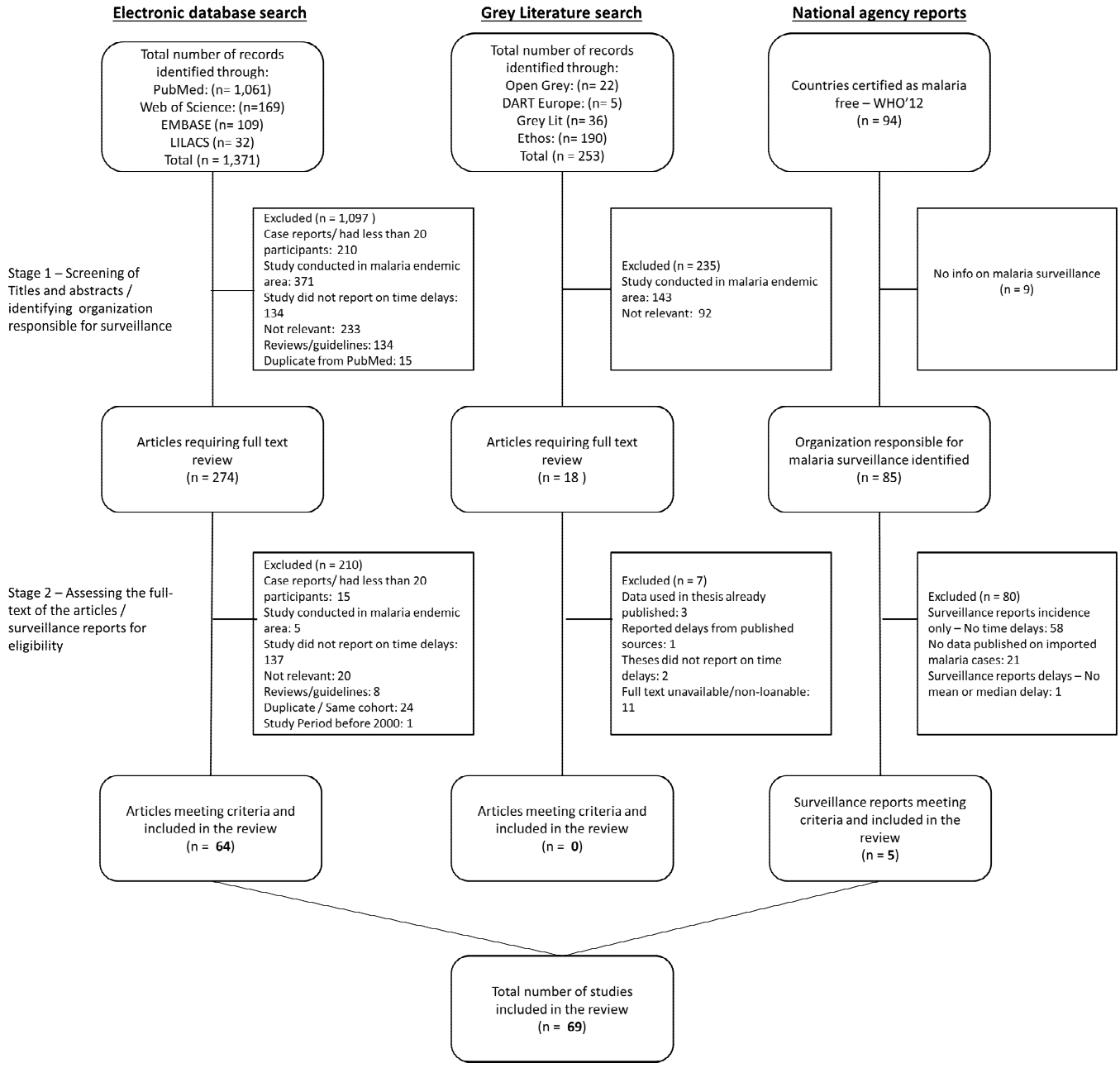

Figure 2. Flowchart of included studies

In terms of study setting, most were conducted in France (n = 17) followed by Spain (n = 8), the UK (n = 6) and the US (n = 4) (appendix A.3). Studies from the USA and France, which reported national

surveillance data, had the largest number of participants. In terms of parasite species, studies which report data for *P. falciparum* and *P. vivax* had a larger number of participants compared to *P. ovale* and *P. malariae*.

The number of studies contributing data to each of the time points included in this review, and the range of reported median and mean duration for those time points by parasite species is summarised in (appendix A.4). Additionally, data were available for 96 patient groups from 28 studies that had reported both a median and IQR for TOS, DD and PD. There were limited data available for MDD, MTD and TD.

Time to the onset of symptoms after return from travel

The TOS for studies that reported both a median and an IQR is summarised in a box plot (Figure 3). This shows that, the median time to onset of symptoms is longer in those who had contracted non falciparum malaria compared to those who had contracted falciparum malaria. Additionally, the wider IQR amongst the non-falciparum patient groups indicates greater variability on when symptoms can first appear after return from travel, compared to the falciparum patient groups.

Amongst the non-falciparum studies, the majority of the patient groups with *P. malariae* had a shorter reported median for the TOS compared to *P. vivax* and *P. ovale*. For *P. ovale* specifically, the smallest and largest medians were reported in 2 patient groups within the same study [11]. In this study, the TOS was reported separately for the 2 subspecies of *P. ovale*; *P. ovale curtisi* (a) and *P. ovale wallikeri* (b), whereas the other included studies for *P. ovale* reported the data for both subspecies together.

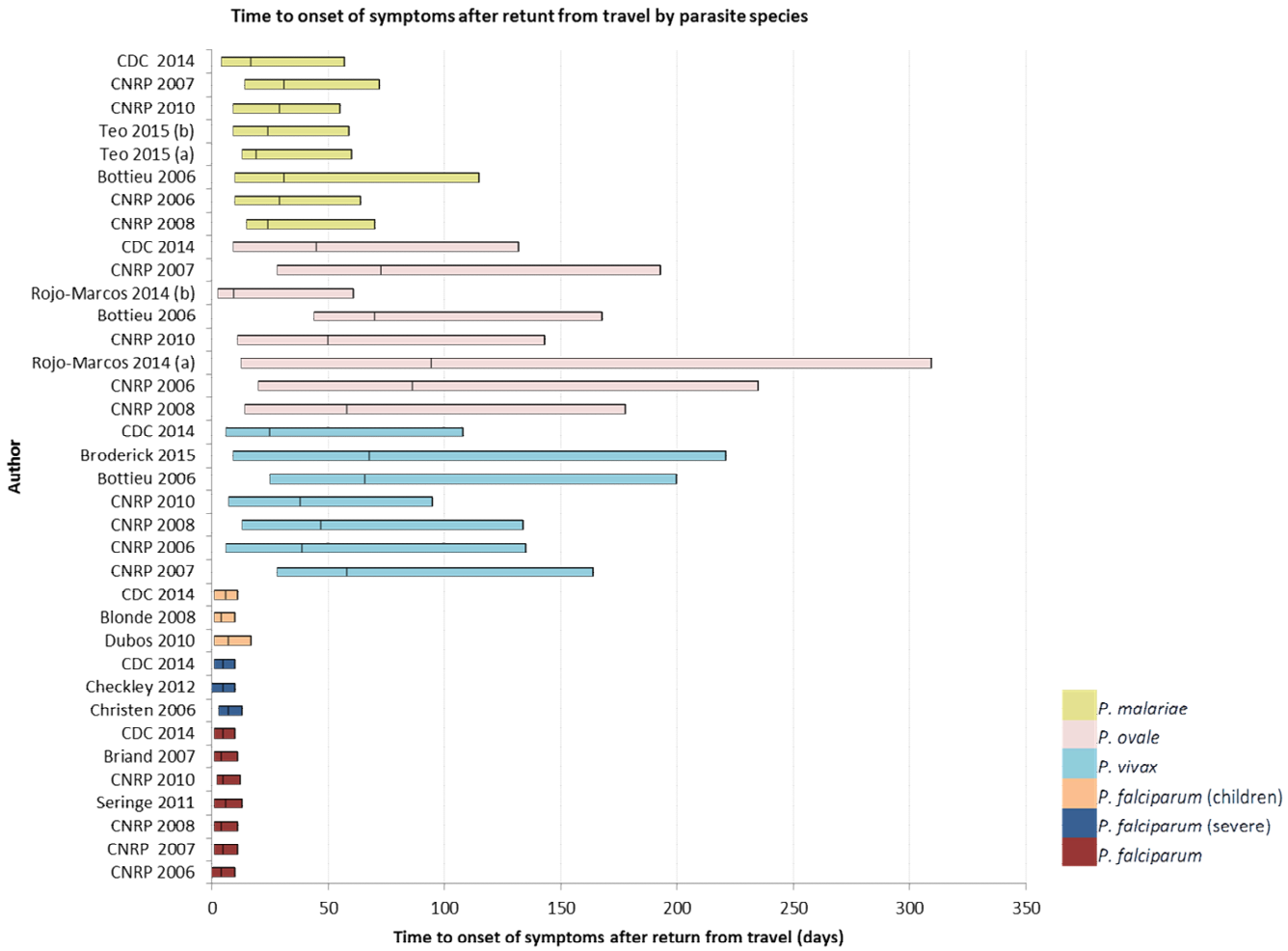

Figure 3. A summary of the TOS in studies which have reported both the median and the IQR. The central line represents the median and the box represents the IQR.

Diagnostic Delay

The DD for studies that reported both a median and an IQR is summarised in (Figure 4). This shows that, amongst these studies, there is no considerable difference in the median DD between the different parasite species (range 3 to 9 days), except for the study by Alaya-Bouafif et al. which reported a larger median delay. In this study, DD was compared between Tunisians (14 days) and non-Tunisians (12.5 days) regardless of Plasmodium species [12].

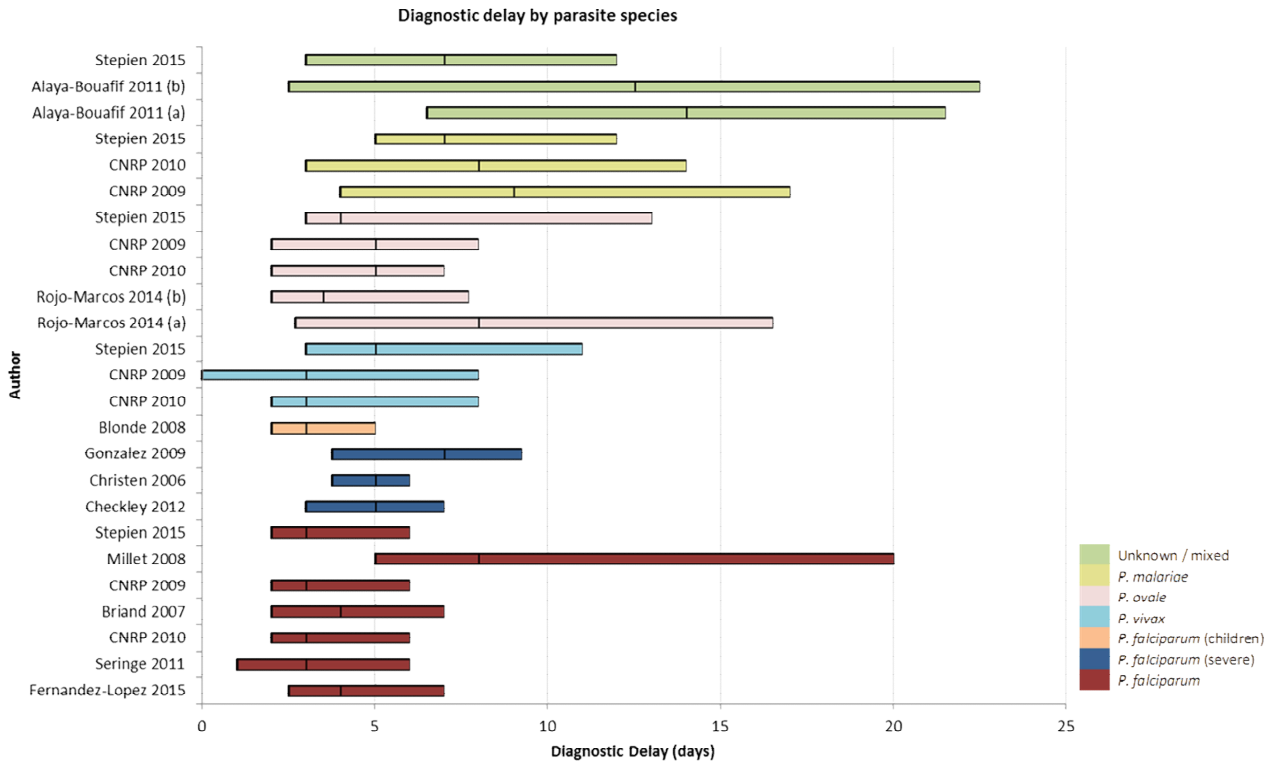

Figure 4. A summary of DD in studies which have reported both the median and the IQR. The central line represents the median and the box represents the IQR.

Patient Delay

The PD for studies that reported both a median and an IQR is summarised in (Figure 5). In these studies, the median PD is comparable for most parasite species (2 to 6 days) except for *P. malariae* where the medians for the PD are comparatively larger (7 to 9 days).

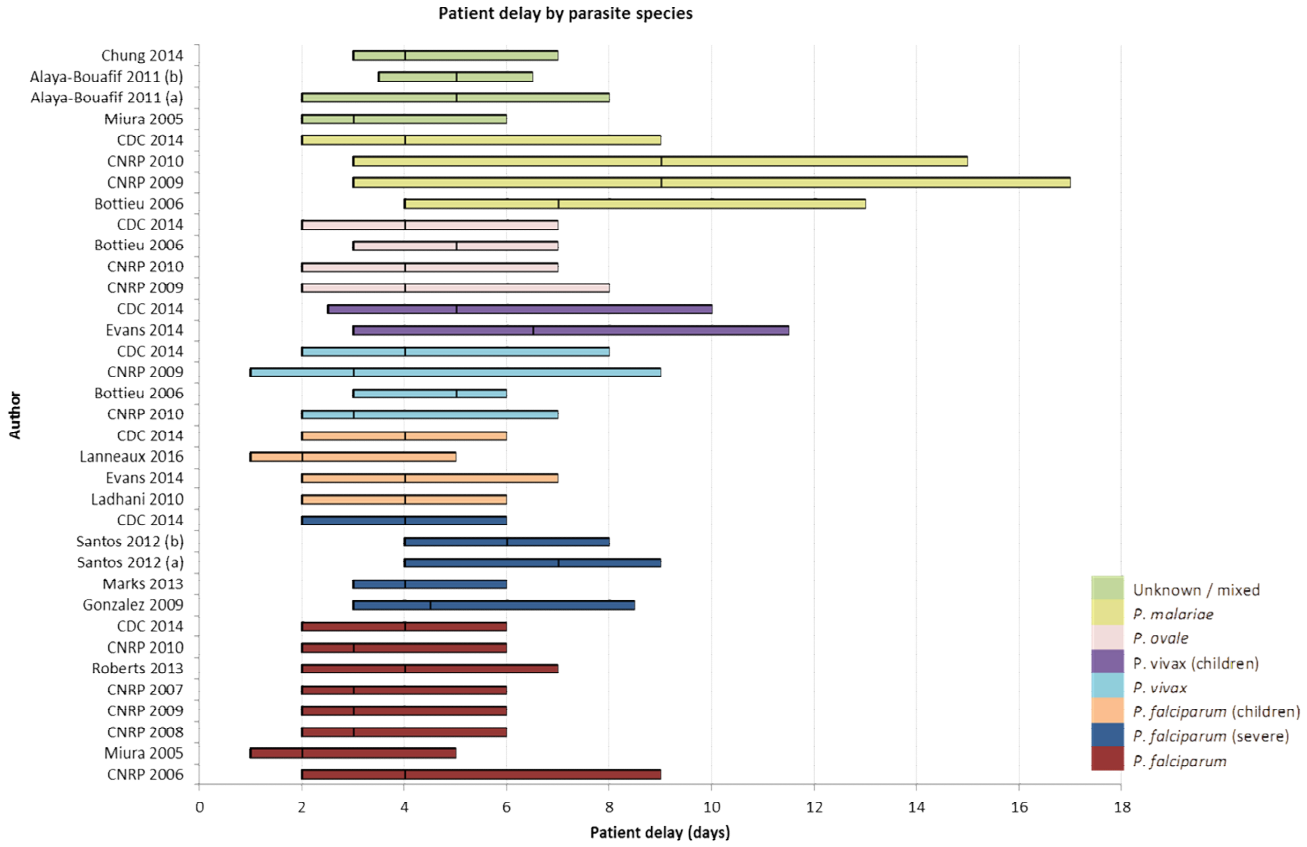

Figure 5. A summary of PD in studies which have reported both the median and the IQR. The central line represents the median and the box represents the IQR.

For both *P. falciparum* and *P. vivax*, the median PD and DD were similar in the studies which reported a median and were included in the review (Figure 6). For *P. falciparum*, the overall median DD was 3.25 days and median PD was 3 days. For *P. vivax*, the overall median DD was 3.75 days and median PD was 4 days.

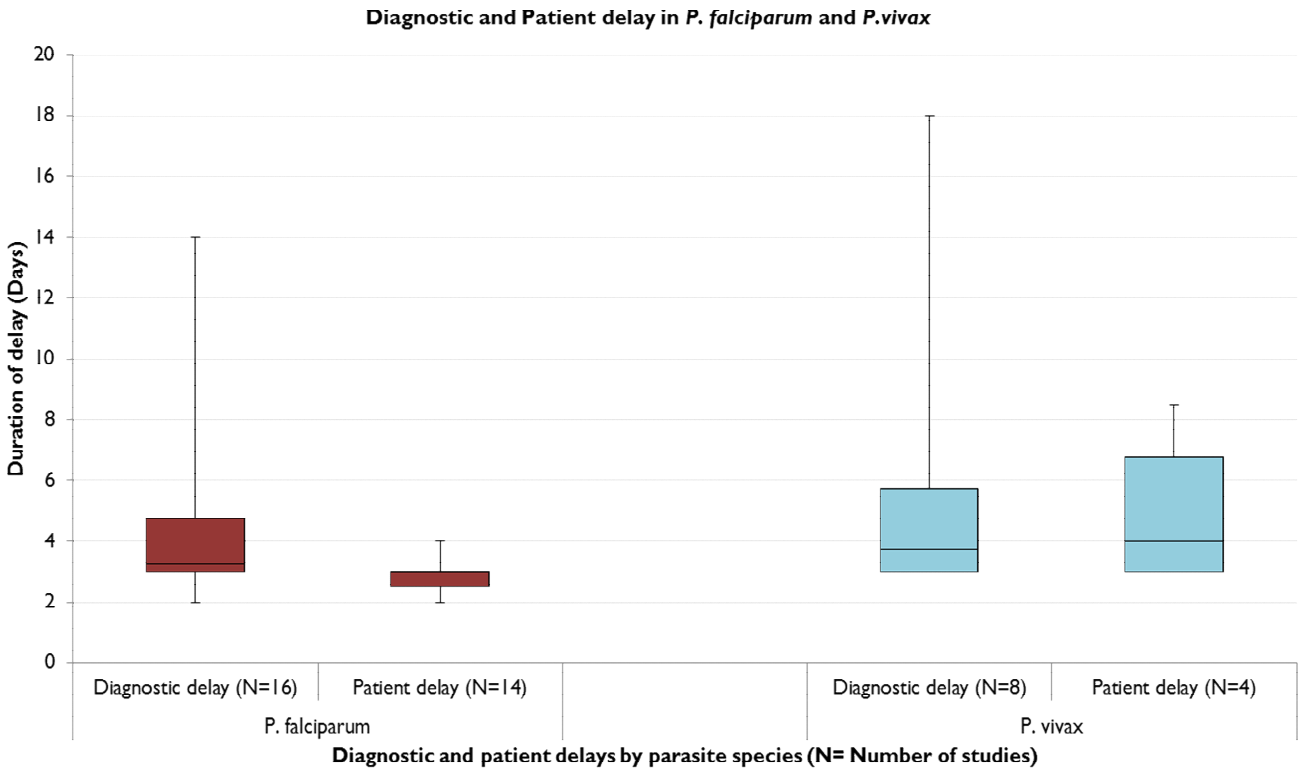

Figure 6. A box and whisker plot summarising the median reported PD and DD for P. falciparum and P. vivax amongst the studies that had reported a median. The boxplots show the median (central line), IQR (boxes) and range (whiskers) of the reported medians

Medical diagnostic delay

There was limited data available amongst the included studies on MDD. A total of 5 studies reported MDD for 7 different patient groups. Data were available for *P. falciparum* (n = 1), severe *P. falciparum* (n = 1), *P. falciparum* in children (n = 2), *P. vivax* (n = 1) and mixed species (n =2) (appendix A.4).

The median reported MDD for all *P. falciparum* groups was 0 days with 3 studies reporting a mean MDD of between 0.7 and 1.5 days. For *P. vivax* and mixed species, the reported median MDD ranged from 4 to 7.5 days, and the mean MDD from 4.6 to 8.8 days.

Treatment delay

Only 2 included studies reported data on treatment delay (appendix A.5).

One study reported a mean TD of 4 days for those who had uncomplicated *P. falciparum* [13]. The second study reported a median TD of 1.5 days for patients with severe malaria that was fatal and 4.5 days for those that recovered [14].

Medical treatment delay

Similar to MDD, there was limited data available amongst the included studies for MTD. A total of 5 studies reported MTD for 6 different patient groups. Data were available for *P. falciparum* (n = 2), severe *P. falciparum* (n = 1), *P. falciparum* in children (n = 1), *P. vivax* (n = 1) and mixed species in children (n =1) (appendix A.5).

All studies reported a median MTD of less than 1 day for all patient groups except for the study by Maltezou et al, which reported a median MTD of 2 days for children with malaria (mixed) [15].

Discussion

Our systematic review showed that there are considerable time delays in the diagnosis of malaria in non-endemic countries. Delays in seeking healthcare by patients accounted for a large proportion of the overall diagnostic delay; however there was limited evidence on delays to diagnosis and treatment after attending a healthcare facility. Furthermore, the review also showed that symptoms can manifest up to a year after return from travel.

Although there is no clear consensus of what is considered an acceptable duration for diagnostic delay, a study by Seringe et al. showed that a DD of between 4 and 12 days is associated with an increased risk of developing severe disease for *P. falciparum* [16]. In the absence of a defined lower limit for DD and given that even those with prompt health seeking after symptom onset, and early diagnosis after presentation, will have some degree of delay, we used a working definition for DD to be greater than 4 days. In our review, 5 out of 14 studies reported a median DD of 4 days or greater for *P. falciparum*, suggesting that improvements in diagnosis could potentially reduce the number of people who develop severe disease in these centres [17], [18], [19], [20], [21]. Interestingly, in the 4

studies which specifically looked at patients with severe *P. falciparum* only, the reported median DD was greater than 4 days in all of them (median DD ranged from 5 to 7 days) [22], [23], [24], [25].

In relation to where the greatest delays occur, our findings suggest that patient factors result in the greatest delays in diagnosis since the median duration for PD and DD were similar. However, the lack of information on other delays (medical diagnostic delay, treatment delay and medical treatment delay) and the retrospective nature of the studies included in this review could have resulted in an overestimation for the true value for PD. This is because information regarding previous healthcare visits, either to other hospitals or to a primary care physician, might not have been considered as patient delay was estimated from symptom onset to attending the facility where the data were collected in some studies [26]. Furthermore, the overestimation of PD would thus result in an underestimation for data related to MDD since the previous healthcare visits which were not considered would shorten the duration for PD and prolong it for MDD. This degree of underestimation could be considerable, since several studies that have specifically looked at previous visits to primary care and other non-specialist centres have reported a large proportion of misdiagnosis of 61% and 80% in these settings. Moreover, a study by Dorsey et al which had looked at malaria misdiagnosis showed that a missed diagnosis resulted in a mean delay in therapy of 5.6 days [26], [27], [28].

Although not an actual delay, given the individual is asymptomatic during this period and would have no reason to seek healthcare, the time to onset of symptoms after return to travel was included in the review since increased understanding on when malaria symptoms develop after return from travel can increase awareness for those working in primary care on when to consider a diagnosis of malaria. Our results corroborate current recommendations to consider a diagnosis of malaria up to a year after returning from a malaria endemic country since the largest value for the 75th percentile of TOS in any of the included studies was 297 days [11], [29].

Other findings of the review reflect existing evidence on the variations in clinical presentation due to the different parasite species. These include; a longer duration until onset of symptoms for *P. vivax* and *P. ovale* since their lifecycle consists of dormant liver stage parasites (hypnozoites), and, a prolonged duration for seeking healthcare in those with *P. malariae* compared to other species, possibly due to the milder form of illness making those affected less likely to seek healthcare earlier [30], [31], [32].

It was difficult to make cross country comparisons given the variation in population characteristics, traveller profiles and service delivery within the same country. For example, Fernandez-Lopez (2015) reported a median diagnostic delay of 4 days (IQR: 2.5 -7) in 185 cases diagnosed in Fuenlabrada, Spain, whereas, Millet (2008) reported a median diagnostic delay of 8 days (IQR: 5 - 20) in Barcelona, Spain [19], [21]. This difference could be attributable to the increased clinical suspicion for malaria due to the high incidence of malaria seen at the hospital in Fuenlabrada, an area with a large immigrant population from endemic areas (99.4% of cases VFR or recently arrived immigrants in Fuenlabrada vs. 54.3% in Barcelona). This hospital had also adopted universal testing of all attendees who are originally from Sub-Saharan Africa resulting in an earlier diagnosis compared to Barcelona [21].

The assembly of data from different publicly available sources resulted in a large number of included studies, allowing comparison of delays by parasite species. However the variations in the characteristics of the reported data and the reporting of medians due to the skewed nature of the data on delays meant that a meta-analysis could not be done and thus the sample size of each study is not reflected in the results (Figures 3, 4 and 5). Therefore when interpreting data from the graphs in the results it is important to take into account the sample sizes which are reported in (Appendix A.5).

Since diagnostic delays are still common in non-endemic countries; strategies to reduce both the patient and healthcare factors should be promoted. This can include encouraging travellers to seek

pre-travel health advice; which can inform them on recognising malaria symptoms and to seek healthcare promptly [33]. Additionally, reminding travellers and healthcare providers that malaria symptoms can develop up to 1 year after return from travel could make the travellers more likely to disclose their travel history and healthcare providers more likely to consider a diagnosis of malaria if symptoms arise within that period. Other strategies that identify cases in the absence of clinical suspicion should be considered as well. For example, modern haematology analysers have been used to detect malaria from tests done routinely in the work-up of a febrile patient. This could prompt further malaria specific investigations in otherwise unsuspected cases and thus reducing DD in these individuals [34].

Finally, the findings of this review also suggest that further evaluation of MDD is needed since the retrospective nature of the studies included in this review may have resulted in its underestimation. One method of evaluating this prospectively is to use routinely collected data from electronic health records to investigate the provision of healthcare in primary care prior to when a diagnosis is made.

Contributors

HB conceived the study. HB, LM, JAC and GR developed the search strategy. HB and JC undertook collection of data from electronic databases and surveillance reports and extracted relevant data. HB implemented the data processing and analysis. HB, JAC and GR contributed to the design of the study and interpretation of the results. All authors contributed to the writing and editing of the drafts.

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HB is currently undertaking a PhD at University College London and is funded by the Ministry of Health, Kuwait. They had no role in study design; data collection, analysis, or interpretation; or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of Interests

We declare no competing interests

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Appendix A

Contents

A.1. Search strategy

Electronic database search

The databases used for the electronic database search were: PubMed, Web of Science, EMBASE and LILACS.

The search terms used to identify relevant articles were developed based on a modified version of the PICO (Participant/ Intervention/ Comparison/ Outcome) search strategy. [1] The "Comparison" component of this search strategy was not relevant given the descriptive nature of the review; however, since the review focuses on the diagnosis and treatment of malaria in the non-endemic setting, a component with search terms related to this setting were added instead. The full search strategy used for the electronic database search is summarised in the table below:

The following search terms were used for the PubMed, Web of Science and EMBASE searches:

Population: Patients diagnosed with malaria	Malaria OR falciparum OR vivax OR plasmodium
AND	
Intervention: Diagnosis or treatment	diagnosis OR diagnostic OR evaluation OR therapy OR treatment OR care OR symptom*
AND	
Setting: Non-endemic	imported OR travel* OR non-endemic OR return*
AND	
Outcome: Delay	delay* OR missed OR day OR days OR duration OR time* OR onset OR age

Additional limits:

- Studies published after 1st of January 2005
- Both the Web of science and EMBASE searches excluded studies which were indexed in Medline

For LILACS, the reduced number of articles indexed in it compared to the other electronic databases meant that searching for all the four components described above yielded no results. Therefore, to broaden the search, the terms “imported” and “malaria” was used for the LILACS database search.

Grey literature database search

To identify conference proceedings, theses and other unpublished articles and reports with potentially relevant data, the following grey literature databases were searched:

- For conference proceedings, the Web of Science core collection database was searched and the search was restricted to identify conference proceedings only.
- For theses, the DART-Europe E-theses portal, the e-theses online service by the British Library (EThOS) and the System for information on Grey Literature in Europe (Open Grey) databases were searched.
- To identify other unpublished health related articles and reports, the Grey Literature Report archives (GreyLit) was searched.

The reduced number of articles indexed in the grey literature databases compared to the electronic databases meant that searching for all the 4 components described previously yielded no results. Therefore, to broaden the search, the terms “imported” and “malaria” was used for the grey literature databases.

National agency reports

Malaria is a notifiable disease in a number of non-endemic countries and statistics related to imported malaria within those countries is usually summarised into annual reports. The agencies responsible for reporting data on malaria differ in each of the non-endemic countries and can include national laboratories, ministries of health, institutes of public health and various other governmental agencies. To search for publicly available reports, firstly, the agency responsible for compiling and reporting malaria statistics in each non-endemic country was identified. Secondly, once identified, their website was searched to obtain any publicly available datasets, reports or summary statistics on malaria cases. Finally, once the summary statistics for the imported malaria cases was obtained, the data reported were reviewed and were included if information on time delays in the diagnosis and treatment of malaria were available. A summary of the reporting agency for each of the non-endemic countries as well as the type of data available is summarised below.

Summary of malaria reporting agency for each malaria non-endemic country

Table 1 Countries certified as malaria free by the WHO in 2012 and the reporting agency where information on time delays were searched. An (x) indicates that the country was added to the WHO supplementary list in 2012.

Country	Year Certified as malaria Free by WHO	Type of data reported	Reporting agency
Lesotho	x	Unable to access MOH website	Ministry of Health
Mauritius	1973	Surveillance reports incidence. No time delays.	Ministry of Health and Quality of Life
Seychelles	x	Surveillance reports incidence. No time delays.	Ministry of Health
Bahrain	x	Surveillance reports incidence. No time delays.	Ministry of Health
Jordan	x	Surveillance reports incidence. No time delays.	Ministry of Health
Kuwait	1963	Surveillance reports incidence. No time delays.	Ministry of Health
Lebanon	x	Surveillance reports incidence. No time delays.	Ministry of Health
Libya	x	Surveillance reports incidence. No time delays.	Ministry of Health
Morocco	2010	Surveillance reports incidence. No time delays.	Ministry of Health
Qatar	x	Surveillance reports incidence. No time delays.	Ministry of Public Health
Tunisia	x	Data on time delays available (Alaya-Bouafif 2011)	National Observatory of New and Emerging Diseases of Tunisia
United Arab Emirates	2007	Surveillance reports incidence. No time delays.	Ministry of Health
Andorra	x	No surveillance data on malaria	Department of Health
Armenia	2011	Unable to access MOH website	Ministry of Healthcare
Austria	1963	Surveillance reports incidence. No time delays.	Federal Ministry of Health and Women's Affairs
Belarus	x	Surveillance reports incidence. No time delays.	Public Health Services and Medical Science in Belarus
Belgium	1963	Reflab responsible for surveillance. No data available.	National reference laboratory for infectious and tropical diseases
Bosnia and Herzegovina	1973	No info on surveillance	Federal Ministry of Health

Bulgaria	1965	NATIONAL REFERENCE LABORATORY (NRL) for Diagnosis of Parasitic Diseases. Data not available on site.	Ministry of Health
Croatia	1973	Surveillance reports incidence. No time delays.	Croatian Institute of Public Health
Cyprus	1967	No data on imported malaria cases	Ministry of Health
Czech Republic	1963	Surveillance reports incidence. No time delays.	Ministry of Health
Denmark	1963	Surveillance reports incidence. No time delays.	Statens Serum Institut
Estonia	x	Surveillance reports incidence. No time delays.	National Institute for Health Development
Finland	1963	Surveillance reports incidence. No time delays.	National Infectious Diseases Register (NIDR)
France (with exception of French Guiana and the island Mayotte)	x	Data on time delays available	Centre Nationaux de reference de paludisme
Germany	1964	Surveillance reports incidence. No time delays.	Robert Koch Institute
Greece	x	Surveillance reports incidence. No time delays.	Hellenic Center for Disease Control & Prevention
Hungary	1964	Surveillance reports incidence. No time delays.	National Center for Epidemiology
Iceland	1963	Surveillance reports incidence. No time delays.	Directorate of Health
Ireland	1963	Surveillance reports incidence. No time delays.	Health Protection Surveillance Centre
Israel	x	Surveillance reports incidence. No time delays.	Ministry of Health
Italy	1970	Surveillance reports incidence. No time delays.	L'Istituto Superiore di Sanità
Kazakhstan	x	No info on surveillance	Ministry of Health
Latvia	x	Surveillance reports incidence. No time delays.	Ministry of Health
Lithuania	x	No data on imported malaria cases	Ministry of Health
Luxembourg	x	No info on surveillance	Ministry of Health
Malta	1963	Surveillance reports incidence. No time delays.	Ministry of Health
Monaco	1963	No info on surveillance	Ministry of Health and Social Affairs
Montenegro	1973	Surveillance reports incidence. No time delays.	Centre for Disease Control and Prevention
Netherlands	1970	Surveillance reports incidence. No time delays.	National Institute for Public Health and the Environment
Norway	1963	Surveillance reports incidence. No time delays.	Norwegian Surveillance System for Communicable Diseases (MSIS)

Poland	1967	Author contacted - Data on time delays available	National Institute for Public Health
Portugal	1973	No access to surveillance data	National Health Service
Republic of Moldova	x	Surveillance reports incidence. No time delays.	Ministry of Health
La Réunion, France	1979	Data on time delays available	Agence de Sante ocean Indien
Romania	1967	No data on imported malaria cases	National Centre for Public Health Information and Statistics
Russian Federation	x	No data on time delays	Federal Service for service of consumer protection and welfare
San Marino	1963	No info on surveillance	Ministry of Health
Serbia	1973	Surveillance reports incidence. No time delays.	Institute of Public Health of Serbia
Slovakia	1963	No data on imported malaria cases	Epidemiological Information System
Slovenia	1973	Surveillance reports incidence. No time delays.	Institute of Public Health of Republic of Slovenia
Spain	1964	Surveillance reports incidence. No time delays.	Instituto de salud carlos III
Sweden	1963	Surveillance reports incidence. No time delays.	National Institute of Public Health
Switzerland	1963	Surveillance reports incidence. No time delays.	Federal Office for Public Health
The former Yugoslav Republic of Macedonia	1973	Surveillance reports incidence. No time delays.	Republic Institute for Health Protection
Turkmenistan	2010	No info on surveillance	Ministry of Health
Ukraine	x	Surveillance reports incidence. No time delays.	Ministry of Health
United Kingdom	1963	Surveillance reports incidence. No time delays.	PHE / Malaria Reference Laboratory
Antigua and Barbuda	x	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Bahamas	x	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Barbados	1968	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Canada	1965	Surveillance reports incidence. No time delays.	Public Health Agency of Canada
Chile	1968	Surveillance reports incidence. No time delays.	Department of Statistics and Health Information
Cuba	1973	Surveillance reports incidence. No time delays.	Institute of Tropical Medicine 'Pedro Kouri'
Dominica	1966	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Grenada	1962	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Jamaica	1966	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency

Saint Kitts and Nevis	x	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Saint Lucia	1962	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Saint Vincent and the Grenadines	x	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
Trinidad and Tobago	1965	Surveillance reports incidence. No time delays.	Caribbean Public Health Agency
United States of America	1970	Author contacted - Data on time delays available	National Malaria Surveillance System through CDC
Uruguay	x	Surveillance reports incidence. No time delays.	Ministry of Health
Venezuela (Bolivarian Republic of, northern part)	1961	Surveillance reports incidence. No time delays.	Ministry of Public Health
Maldives	x	No data on imported malaria cases	Ministry of Health
Australia	1981	Surveillance reports incidence. No time delays.	National Notifiable Diseases Surveillance System
Brunei Darussalam	1987	No data on imported malaria cases	Ministry of Health
China, Taiwan	1965	Surveillance reports incidence. No time delays.	Center for Disease Control
Cook Islands	1963	No data on imported malaria cases	Ministry of Health
Fiji	1963	No data on imported malaria cases	Ministry of Health
Japan	x	Surveillance reports incidence. No time delays.	National Institute of Infectious Diseases
Kiribati	x	No data on imported malaria cases	Ministry of Health
Marshall Islands	1963	No data on imported malaria cases	Economic Policy, Planning and Statistic Office
Micronesia (Federated States of)	1963	No data on imported malaria cases	Department of Health and social affairs
Mongolia	1963	No data on imported malaria cases	National Center for Infectious Diseases
Nauru	1963	Surveillance reports incidence. No time delays.	International Health and Medical Services (Australia)
New Zealand	1963	Surveillance reports incidence. No time delays.	New Zealand Public Health Observatory
Niue	1963	No data on imported malaria cases	Statistics Niue
Palau	1963	No data on imported malaria cases	Ministry of Health
Samoa	1963	No data on imported malaria cases	Ministry of Health
Singapore	1982	Surveillance reports incidence. No time delays.	Ministry of Health

Tonga	1963	No data on imported malaria cases	Ministry of Health
Tuvalu	x	No data on imported malaria cases	Tuvalu Central statistics division

A.2. Quality Assessment

Methods for Quality Assessment

Two reviewers independently examined the components of each included study for risk of bias. The "JBI critical appraisal checklist for case series" was used since it was anticipated that the majority of the included studies would be case series. [2] Furthermore, since the focus of the review is time to diagnosis or treatment of malaria, the same checklist was used for cohort studies that report on the variables of interest in the baseline characteristics of the sample. Although there are cohort specific "risk of bias" assessment tools (e.g. Newcastle-Ottawa Scale /Downs and Black instrument), the use of the case series checklist is justified since the baseline characteristics of these cohort studies is descriptive.[3,4] Any longitudinal and intervention related effects were not considered and the data extracted from the studies comprised of only cases and was treated like a case series.

The checklist comprises of 10 items addressing the possibility of bias in the design, conduct and analysis of case series studies. For each item, the reviewers assigned a "yes", "no" or "unclear" on whether the item in question had been addressed in the study. A guidance tool with criteria on what comprises a "yes" or "no" answer was given to each of the reviewers. Discrepancies between the reviewers (HB and JC) were resolved by consensus, and if necessary, a third party (GR) was consulted.

Each of the included studies was given a score out of 10, with 1 point awarded for each "yes" answer. This results in a scale; with a score of 10/10 having the lowest risk of bias and 0/10 having the highest risk of bias.

Results of quality assessment

Most of the included studies had a clear inclusion criteria and the cases consisted of a lab confirmed diagnosis of malaria, either by microscopy or antigen based testing, ensuring that the diagnosis of malaria was reliable and objective (Questions 1, 2 and 3). In one third of the included studies the selection of cases was not consecutive (26/69) and not all eligible cases were included (27/69), and thus, would make these studies prone to selection bias (Questions 4 and 5). Most of the included studies (67/69) provided clear information on the demographic and relevant clinical information of the cases and therefore the risk of reporting bias within the included studies is low (Question 6 and 7). In 26/69 studies follow-up data of the cases were not available, however, since this review mainly focuses on data prior to diagnosis and treatment, subsequent information regarding morbidity and mortality does not have an effect on this review (Question 8). Information regarding the site where the malaria cases presented was not available in 22/69 studies (Question 9) and therefore information on PD, MDT and MTT within these studies might not be accurate since visits to a healthcare provider prior to attending the reporting site might not have been considered, the implications of this on the review are described in the discussion section. Finally, 10/69 studies reported a median or mean delay with no measure of spread (IQR/SD) making it difficult to infer the dispersion of reported delays within these studies (Question 10).

Table summarising the results of the quality assessment

Author	Year	Were there clear criteria for inclusion?	Was the condition measured in a standard, reliable way for all participants included in the case series?	Were valid methods used for identification of the condition for all participants included in the case series?	Did the case series have consecutive inclusion of participants?	Did the case series have complete inclusion of participants?	Was there clear reporting of the demographics of the participants in the study?	Was there clear reporting of clinical information of the participants?	Were the outcomes or follow up results of cases clearly reported?	Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	Was statistical analysis appropriate?	Overall score
Yeruva	2016	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	No	7
Calvo-Cano	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Teo	2015	Yes	Yes	Yes	No	No	No	Unclear	Yes	No	Yes	5
Jaureguiberry	2015	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	yes	7
McCarthy	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	9
Broderick	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	8
Thompson	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Chung	2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Grynberg	2015	Yes	Unclear	Unclear	No	No	Yes	Yes	Yes	Yes	Yes	6
Dakic	2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	8
Evans	2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Odolini	2014	Yes	Unclear	Unclear	No	No	Yes	Yes	No	No	Yes	4
Stepien	2003 - 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	9
Rojo-Marcos	2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	9
Nakayama	2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Cordel	2013	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Demaison	2013	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	7
Maltezou	2013	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Marks	2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Roberts	2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Camburn	2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	9
Rossi	2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9
Santos	2012	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Checkley	2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	8
Ramirez-Olivencia	2012	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Antinori	2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10

Phares	2011	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes	6
Minodier	2011	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Seringe	2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Rey	2010	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	No	6
Bruneel	2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Arnaez	2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Ladhani	2010	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	7
Pistone	2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	8
Gonzalez	2009	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Dubos	2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Goldfarb	2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Leahy	2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9
Khan	2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Thierfelder	2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Millet	2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	8
Blonde	2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Briand	2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Jennings	2006	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Christen	2006	Yes	Yes	Yes	No	No	Yes	Yes	Unclear	No	Yes	6
Uzzan	2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Bottieu	2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Vatan	2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Chalumeau	2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Parola	2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	8
Badiaga	2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Askling	2005	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes	6
Miura	2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Kitchener	2005	Yes	Unclear	Unclear	No	No	Yes	Yes	Yes	No	No	4
Ben-Ami	2005	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Unclear	Yes	7
Charles	2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	9
Fernandez-Lopez	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Kuna	2015	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Subelj	2012	Yes	Yes	Yes	No	No	Yes	Yes	No	No	Yes	6
Higa	2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Soraa	2006	Yes	Yes	Yes	No	No	Unclear	Unclear	Unclear	Yes	Yes	5
CNRP	2006 - 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	8
Alaya-Bouafif	2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	8
D'Ortenzio	2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	7
Bouchaud	2012	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No	7
Lanneaux	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10
Hickey	2011	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9
Rabe	2005	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7
CDC	2003 - 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	8

A.3. Number of studies contributing data for this review from each country

Table 2. A table listing the number of studies included in the review from each country

Country	Number of studies
France	17
Spain	8
UK	6
USA	4
Australia	3
Canada	3
Japan	3
Multicentre	3
Switzerland	3
Israel	2
Poland	2
Tunisia	1
Belgium	1
Germany	1
Greece	1
Ireland	1
Italy	1
Le Reunion	1
Morocco	1
New Zealand	1
Portugal	1
Qatar	1
Serbia	1
Singapore	1
Slovenia	1
Sweden	1

A.4. Overall summary of results for all study outcomes

Table 3 This table summarises the range of reported median and mean duration for the Time to Onset of Symptoms (TOS), diagnostic delay (DD), patient delay (PD), medical diagnostic delay (MDD), treatment delay (TD) and medical treatment delay (MTD) from all studies included in the review.

		Number of studies reporting median	Range of reported median duration (days)	Number of studies reporting mean	Range of reported mean duration (days)	Number of studies reporting median and IQR and included in the boxplot graphs
TOS	*P. falciparum*	14	3 to 14	9	5.2 to 15.1	7
	P. falciparum (severe)	5	5 to 7	1	7.9	3
	P. falciparum (children)	4	2 to 7	1	11.7	3
	P. vivax	14	28 to 240	9	61 to 282	7
	P. vivax (children)	0	-	0	-	0
	P. ovale	10	9.5 to 87	7	89.3 to 171.4	8
	P. malariae	9	19 to 31	7	40.6 to 142.9	8
	mixed	0	-	0	-	0
	mixed (children)	2	32 to 52	0	-	0
DD	*P. falciparum*	15	2 to 8	9	4 to 12.5	7
	P. falciparum (severe)	4	5 to 7	3	3.1 to 6.2	3
	P. falciparum (children)	4	2 to 4	2	4.7 to 5	1
	P. vivax	6	3 to 5	3	6.5 to 18.3	3
	P. vivax (children)	0	-	1	3	0
	P. ovale	6	3.5 to 8	3	6.4 to 13	5
	P. malariae	3	7 to 9	3	14.3 to 19.8	3
	mixed	5	3 to 18	3	6.6 to 24	3
	mixed (children)	0	-	0	-	0
PD	*P. falciparum*	13	2 to 4	10	2.4 to 15.3	8
	P. falciparum (severe)	8	3 to 7	2	4.2 to 5.6	5
	P. falciparum (children)	8	1 to 5	2	3.1 to 5.7	4
	P. vivax	5	3 to 8.5	4	3.6 to 16.7	4
	P. vivax (children)	2	5 to 6.5	1	10	2
	P. ovale	5	3 to 5	3	6.7 to 9.3	4
	P. malariae	4	4 to 9	3	8.1 to 15.6	4
	mixed	4	3 to 5	1	4.7	4
	mixed (children)	1	2	0	-	0
MDD	*P. falciparum*	0	-	1	0.7	-
	P. falciparum (severe)	1	0	1	1.3	-
	P. falciparum (children)	2	0	1	1.5	-
	P. vivax	0	-	1	4.6	-
	P. vivax (children)	0	-	0	-	-
	P. ovale	0	-	0	-	-
	P. malariae	0	-	0	-	-
	mixed	2	4 to 7.5	2	5.8 to 8.8	-
	mixed (children)	0	-	0	-	-
TD	*P. falciparum*	0	-	1	4	-
	P. falciparum (severe)	2	1.5 to 4	0	-	-
	P. falciparum (children)	0	-	0	-	-
	P. vivax	0	-	0	-	-
	P. vivax (children)	0	-	0	-	-
	P. ovale	0	-	0	-	-
	P. malariae	0	-	0	-	-
	mixed	0	-	0	-	-
	mixed (children)	0	-	0	-	-
MTD	*P. falciparum*	1	<1	1	0	-
	P. falciparum (severe)	1	0.1	1	1.2	-
	P. falciparum (children)	1	0.2	0	-	-
	P. vivax	0	-	1	0.3	-
	P. vivax (children)	0	-	0	-	-
	P. ovale	0	-	0	-	-
	P. malariae	0	-	0	-	-
	mixed	0	-	0	-	-
	mixed (children)	1	2	0	-	-

A.5. Characteristics of the studies included in the systematic review

The characteristics and reported outcomes of the studies included in the review are summarised below. Key: (*) = mean, (SD) = Standard Deviation, (IQR) = Interquartile range. Ranges are reported in brackets.

Time to the Onset of Symptoms (TOS)

P. falciparum

Study author (ref)	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	TOS (days)
Yeruva [5]	2016	Retrospective chart review	USA	1998-2012	Patients with a positive blood smear for malaria	37	84	8*
Dakic [6]	2014	Retrospective chart review	Serbia	2010-2014	CCS parasitology lab cases malaria (*falciparum*)	32	100	7·8* +/- 6·9 (0-30)
Camburn [7]	2012	Prospective Observational Study	New Zealand	2008-2009	Laboratory confirmed cases *falciparum* malaria	18	100	3 (0-26)
Antinori [8]	2011	Retrospective chart review	Italy	1997-2007	Smear +ve *falciparum*	228	100	6
Phares [9]	2011	Retrospective chart review	USA	2007-2008	*P. falciparum* in refugees who received treatment for malaria	39	100	14 (3-46)
Seringe [10]	2011	Retrospective chart review	France	1996-2003	All patients with *P. falciparum* who were reported to CNRP	21,888	100	6 (IQR 1-12)
Khan [11]	2009	Retrospective chart review	Qatar	2005	Lab confirmed *P.falciparum*	34	100	14 (1-39)
Briand [12]	2007	Retrospective chart review	France	1993-2000	Lab confirmed *P. falciparum*	400	100	4 (IQR 1-10)
Ben-Ami [13]	2005	Retrospective questionnaire	Israel	1999-2001	Laboratory confirmed *P. falciparum* without chemoprophylaxis	22	100	14 (7-30)
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. falciparum*	14	100	5·2 days “average” (0-15)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.falciparum*	1725	100	9* (SD 25·2) 5 (IQR 2-10)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.falciparum*	1310	100	12·8* (SD 61·3) 6 (IQR 2-11)
CNRP [15]	2008	National Surveillance data	France	2008	Notified cases of *P.falciparum*	1609	100	10·5* (SD 1·6) 4 (IQR 1-10)
CNRP [15]	2007	National Surveillance data	France	2007	Notified cases of *P.falciparum*	1481	100	15·1* (SD 120·8) 5 (IQR 1-10)
CNRP [15]	2006	National Surveillance data	France	2006	Notified cases of *P.falciparum*	1973	100	7·0* (SD 35·1) 4 (IQR 0-10)
D'Ortenzio [16]	2008	National Surveillance data	Le Reunion	2003-2007	All reported cases of malaria in Reunion	617	84·3	7
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. falciparum* cases reported to the CDC	5637	100	9·6* (SD35·1) 5 (IQR 1-10)

P. falciparum (Severe)

Study author	Year	Study design	Country	Study period	description of study participants	Sample size	% *P.falciparum*	TOS (days)
McCarthy [18]	2015	Retrospective chart review	Canada	2001-2013	Patients with severe malaria	248	94	7
Checkley [19]	2012	Retrospective chart review	UK	1987-2006	Fatal cases of malaria	135	100	5 (IQR 0-10)
Christen [20]	2006	Retrospective chart review	Switzerland	1988-2002	Fatal cases of malaria	33	100	7 (IQR 3-10)
Badiaga [21]	2005	Retrospective chart review	France	1996-2002	Patients >15 years admitted with severe malaria (*P.falciparum*)	42	100	5 (0-21)
CDC[17]	2017	National Surveillance data	USA	2003-2014	Severe *P. falciparum* cases reported to the CDC	1123	100	7·9* (SD 24·9) 5 (IQR 1-10)

P. falciparum (Children)

Study author	Year	Study design	Country	Study period	description of study participants	Sample size	% *P.falciparum*	TOS (days)
Minodier [22]	2011	Prospective observational study	France	2004-2009	Children aged 3 months to 16 years with uncomplicated malaria	95	100	2 (IQR 8·25)
Dubos [23]	2010	Retrospective chart review	France	2000-2006	Children aged 18 and under	120	83	7 (IQR 1-16)
Blonde [24]	2008	Retrospective chart review	France	2004-2005	Lab confirmed *P.falciparum* in Children (<15 years) treated with atovaquone-proguanil	48	100	4 (IQR 1-9)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. falciparum* cases reported to the CDC (aged <18years)	1437	100	11·7* (SD 52·7) 6 (IQR 1-11)

P. vivax

Study author	Year	Study design	Country	Study period	description of study participants	Sample size	% *P.vivax*	TOS (days)
Broderick [25]	2015	observational study	UK	1987-2013	Patients with *P. vivax*	12,769	100	68 (IQR 9-212)
Dakic [6]	2014	Retrospective chart review	Serbia	2010-2015	CCS parasitology lab cases malaria (*vivax*)	4	100	61* +/- 99·7 (0-210)
Odolini [26]	2014	Retrospective chart review	Multicentre	2005-2012	Eurotravnet database - *P. vivax* imported from Pakistan	45	100	282* (1-41,123)
Demaison [27]	2013	retrospective chart review	France	2000-2009	Lab confirmed *P. vivax*	94	100	49
Camburn [7]	2012	Prospective Observational Study	New Zealand	2008-10	Laboratory confirmed cases of *vivax* malaria	16	100	43 (10-274)
Antinori [8]	2011	retrospective chart review	Italy	1997-2007	Smear +ve non-falciparum	58		73
Khan [11]	2009	retrospective chart review	Qatar	2005	Lab confirmed *P.vivax*	39	100	28 (2-218)
Bottieu [28]	2006	retrospective chart review	Belgium	2000-2005	Lab confirmed *P.vivax*	48	100	66 (IQR 25-175)
Kitchener [29]	2005	retrospective chart review	Australia	1999-2001	Lab confirmed *P. vivax* in Army personnel returning from deployment	241	100	89
Ben-Ami [13]	2005	Retrospective questionnaire	Israel	1991-2001	Laboratory confirmed *P. vivax* with prophylaxis	3	100	240 (150-240)
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. vivax*	7	100	85·6 "average" (2-295)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.vivax*	106	100	70·6* (SD 84) 38 (IQR 7-88)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.vivax*	132	100	66·7* (SD 133·4) 38·5 (IQR 12·5-70·5)
CNRP [15]	2008	National Surveillance data	France	2008	Notified cases of *P.vivax*	85	100	89·1* (SD 12·0) 47 (IQR 13-121)
CNRP [15]	2007	National Surveillance data	France	2007	Notified cases of *P.vivax*	92	100	123·2* (SD 251·1) 58 (IQR 28-136)
CNRP [15]	2006	National Surveillance data	France	2006	Notified cases of *P.vivax*	119	100	111·6* (SD 258·5) 39 (IQR 6-129)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P.vivax* cases reported to the CDC	1607	100	73·3* (SD 109·8) 25 (IQR 6-108)

P. ovale

Study author	Year	Study design	Country	Study period	description of study participants	Sample size	% *P. ovale*	TOS (days)
Dakic [6]	2014	Retrospective chart review	Serbia	2010-2016	CCS parasitology lab cases malaria (*ovale*)	6	100	165* +/-113·1 (72-365)
Rojo-Marcos (a) [30]	2014	retrospective chart review	Spain	2005-2011	Lab confirmed *P. ovale* curtisi	21	100	94·5 (IQR 12·5-297·2)
Rojo-Marcos (b) [30]	2014	retrospective chart review	Spain	2005-2011	Lab confirmed *P. ovale* wallikeri	14	100	9·5 (IQR 2·7-58·2)
Demaison [27]	2013	retrospective chart review	France	2000-2009	Lab confirmed *P.ovale*	77	100	71
Bottieu [28]	2006	retrospective chart review	Belgium	2000-2005	Lab confirmed *P.ovale*	34	100	70 (IQR 44-124)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.ovale*	86	100	122·8* (SD 262·3) 50 (IQR 11-132)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.ovale*	79	100	160* (SD 270·1) 87 (IQR 17-178)
CNRP [15]	2008	National Surveillance data	France	2008	Notified cases of *P.ovale*	75	100	150·8* (SD 34·3) 58 (IQR 14-164)
CNRP [15]	2007	National Surveillance data	France	2007	Notified cases of *P.ovale*	92	100	126·5* (SD 157·8) 73 (IQR 28-165)
CNRP [15]	2006	National Surveillance data	France	2006	Notified cases of *P.ovale*	102	100	171·4* (SD 247·0) 86·5 (IQR 20-215)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. ovale* cases reported to the CDC	253	100	89·3* (SD 124·2) 45 (IQR 9-132)

P. malariae

Study author	Year	Study design	Country	Study period	description of study participants	Sample size	% *P. malariae*	TOS (days)
Dakic [6]	2014	Retrospective chart review	Serbia	2010-2017	CCS parasitology lab cases malaria (*malariae*)	3	100	42·7* +/- 67 (2-120)
Bottieu [28]	2006	Retrospective chart review	Belgium	2000-2005	Lab confirmed *P.malariae*	16	100	31 (IQR 10-105)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.malariae*	37	100	142·9* (SD 668·5) 29 (IQR 9-46)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.malariae*	35	100	47·4* (SD 54·8) 27 (IQR 13-62)
CNRP [15]	2008	National Surveillance data	France	2008	Notified cases of *P.malariae*	42	100	57* (SD 18·8) 24 (IQR 15-55)
CNRP [15]	2007	National Surveillance data	France	2007	Notified cases of *P.malariae*	32	100	40·6* (SD 41·7) 31 (IQR 14-58)
CNRP [15]	2006	National Surveillance data	France	2006	Notified cases of *P.malariae*	38	100	48·4* (SD 72·0) 29 (IQR 10-54)
Teo (a) [31]	2015	Retrospective review	Sweden	1997-2013	Cases *P.malariae* Sweden	20	100	19 (IQR 13-47) (0-70)
Teo (b) [31]	2015	Retrospective review	UK	1991-2010	Cases *P.malariae* UK	248	100	24 (IQR 9-50)(-5 - 1123)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. malariae* cases reported to the CDC	258	100	49·7* (SD 111·6) 17 (IQR 4-57)

Mixed malaria in children

Study author	Year	Study design	Country	Study period	description of study participants	Sample size	% *P. falciparum*	TOS (days)
Thompson [32]	2015	retrospective chart review	Australia	2000-2010	Children aged 16 and under	40	68	32 (4-434)
Maltezou [33]	2013	retrospective chart review	Greece	1972-2012	Children aged 15 and under	22	32	50 (4 days - 16 months)

Diagnostic delay

P. falciparum

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Diagnostic delay (days)
Cordel [34]	2013	prospective observational study	France	2002-2007	Lab confirmed uncomplicated *P.falciparum*	553	100	5 (1-64)
Ramirez-Olivencia [35]	2012	retrospective chart review	Spain	2002-2007	Symptomatic malaria	277	86.4	8·16* (SD 16)
Bouchaud[36]	2012	prospective observational study	Multi centre	2003 - 2009	Uncomplicated *P. falciparum*	504	100	3
Antinori [8]	2011	retrospective chart review	Italy	1997-2007	Smear +ve *P. falciparum*	228	100	3 (0-10)
Seringe [10]	2011	retrospective chart review	France	1996-2003	All patients with *P. falciparum* who were reported to CNRP	21,888	100	3 (IQR 1-6)
Rey [37]	2010	retrospective chart review	Spain	2005-2008	Malaria cases notified to preventative medicine department	57	94·7	4·5
Pistone [38]	2010	retrospective chart review	France	2000-2007	Lab confirmed malaria in those aged > 15 years	488	82	3
Khan [11]	2009	retrospective chart review	Qatar	2005	Lab confirmed *P.falciparum*	34	100	3(2-6)
Thierfelder [39]	2009	retrospective chart review	Switzerland	1994-2004	Those diagnosed with malaria aged >16 years	109	88	4* (0·5-31)
Millet [40]	2008	retrospective chart review	Spain	1989-2005	Lab confirmed malaria notified to Barcelona Public Health Agency	997	71	8 (IQR 5-20)
Briand [12]	2007	retrospective chart review	France	1993-2000	Lab confirmed *P. falciparum*	400	100	4 (IQR 2-7)
Jennings [41]	2006	prospective observational study	UK	2000-2002	Patients admitted to HTD with *P.falciparum* - uncomplicated	74	100	4·29* (1-60)
Uzzan (a) [42]	2006	Preliminary Study	France	2003-2004	Cases *P. falciparum* with raised procalcitonin	6	100	12·5* +/-7·7
Uzzan (b) [42]	2006	Preliminary Study	France	2003-2004	Cases *P. falciparum* malaria without raised procalcitonin	11	100	5·3* +/- 3·1
Fernandez-Lopez [43]	2015	retrospective chart review	Spain	2004-2014	Lab confirmed malaria	185	90·3	4 (IQR 2·5-7)
Soraa [44]	2006	retrospective chart review	Morocco	2001-2004	Lab confirmed malaria	68	85·3	18* (1-90)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P. falciparum*	1,866	100	5·7* (SD 11·5) 3 (IQR 2-6)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.falciparum*	1,644	100	8·8* (SD 92·6) 3 (IQR 2-6)
D'Ortenzio [16]	2008	National Surveillance data	Le Reunion	2003-2007	All reported cases of malaria in Reunion	617	84·3	3
Rabe [45]	2005	retrospective chart review	Germany	1992-2002	Lab confirmed *P. falciparum* (Uncomplicated)	73	100	2 (0-24)
Stepien[46]	2017	National Surveillance data	Poland	2003-2015	Lab confirmed *P. falciparum*	181	100	5·26* (SD 7·2) 3 (IQR 2-6)

P. falciparum (Severe)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Diagnostic delay (days)
Checkley [19]	2012	retrospective chart review	UK	1987-2006	Fatal cases of malaria	146	100	5 (IQR 3-7)
Bruneel (a) [47]	2010	retrospective chart review	France	2000-2006	Adults admitted to ICU with severe malaria + survived	358	100	5·4* (SD 5·1)
Bruneel (b) [47]	2010	retrospective chart review	France	2000-2006	Adults admitted to ICU with severe malaria + died	42	100	6·2* (SD 4·6)
Gonzalez [48]	2009	retrospective chart review	Spain	1991-2007	Adults admitted to ICU with severe malaria	20	100	7 (IQR 3·75-9·25)
Jennings [41]	2006	prospective observational study	UK	2000-2002	Patients admitted to HTD with *P.falciparum* - severe	25	100	3·08* (1-10)
Christen [20]	2006	retrospective chart review	Switzerland	1988-2002	Fatal cases of malaria	33	100	5 (IQR 3·75-6)
Rabe [45]	2005	retrospective chart review	Germany	1992-2003	Lab confirmed *P. falciparum* (Severe)	44	100	5 (0-30)

P. falciparum (Children)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Diagnostic delay (days)
Minodier [22]	2011	prospective observational study	France	2004-2009	Children aged 3 months to 16 years with uncomplicated malaria	95	100	3 (IQR 4·25)
Dubos [23]	2010	retrospective chart review	France	2000-2006	Children aged 18 and under	120	83	2
Blonde [24]	2008	retrospective chart review	France	2004-2005	Lab confirmed *P.falciparum* in Children (<15 years) treated with atovaquone-proguanil	48	100	3 (IQR 2-5)
Chalumeau [49]	2006	prospective observational study	France	2002	Lab confirmed *P. falciparum* in children <18 years	29	100	4 (0-19) 4·7*
Hickey[50]	2011	retrospective chart review	USA	1996-2006	Lab confirmed *P. falciparum* in children <18 years	72	100	5* (SD 5·4)

P. vivax

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.vivax*	Diagnostic delay (days)
Demaison [27]	2013	retrospective chart review	France	2000-2009	Lab confirmed *P. vivax*	94	100	4·5
Antinori [8]	2011	retrospective chart review	Italy	1997-2007	Smear +ve non-falciparum	58	76·2	5 (0-47)
Khan [11]	2009	retrospective chart review	Qatar	2005	Lab confirmed *P.vivax*	39	100	3(1-6)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.vivax*	119	100	6·5* (SD 16·7) 3 (IQR 2-8)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.vivax*	157	100	18·3* (SD 61·1) 3 (IQR 0-8)
Stepien[46]	2017	National Surveillance data	Poland	2003-2015	Lab confirmed *P. vivax*	51	100	8·7* (SD 10·0) 5 (3-11)

P. vivax (Children)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.vivax*	Diagnostic delay (days)
Hickey[50]	2011	retrospective chart review	USA	1996-2006	Lab confirmed *P. vivax* in children <18 years	3	100	3* (SD 2·3)

P. ovale

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.ovale*	Diagnostic delay (days)
Rojo-Marcos (a)[30]	2014	retrospective chart review	Spain	2005-2011	Lab confirmed *P. ovale curtisi*	21	100	8 (IQR 2·7-16·5)
Rojo-Marcos (b)[30]	2014	retrospective chart review	Spain	2005-2011	Lab confirmed *P. ovale wallikeri*	14	100	3·5 (IQR 2·0-7·7)
Demaison[27]	2013	retrospective chart review	France	2000-2009	Lab confirmed *P.ovale*	77	100	4
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.ovale*	98	100	7·8* (SD 18·6) 5 (IQR 2-7)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.ovale*	102	100	13* (SD 50·7) 5 (IQR 2-8)
Stepien[46]	2017	National Surveillance data	Poland	2003-2015	Lab confirmed *P.ovale*	7	100	6·4* (SD 4·9) 4 (IQR 3-13)

P. malariae

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.malariae*	Diagnostic delay (days)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.malariae*	46	100	15* (SD 21·1) 8 (IQR 3-14)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.malariae*	47	100	14·3* (SD 18·2) 9 (IQR 4-17)
Stepien[46]	2017	National Surveillance data	Poland	2003-2015	Lab confirmed *P. malariae*	5	100	19·8* (SD 29·4) 7 (IQR 5-12)

Mixed species / Unknown species

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Diagnostic delay (days)
Charles [51]	2005	Questionnaire	Australia	1990-2001	Cases diagnosed with malaria and notified to Western Australian Notifiable ID register	283	28	3 (0-336)
Subelj [52]	2012	retrospective chart review	Slovenia	2001-2011	Lab confirmed malaria	73	42·5	18 (1-136) 24*
Kuna [53]	2015	retrospective chart review	Poland	2002-2014	Patients admitted to hospital with lab confirmed malaria	82	63·4	6·6* (1-28)
Alaya-Bouafif (a) [54]	2011	National Surveillance data	Tunisia	2002-2007	Notified cases of malaria amongst Tunisian Patients	55	N/A	14 (IQR 15)
Alaya-Bouafif (b) [54]	2011	National Surveillance data	Tunisia	2002-2007	Notified cases of malaria amongst Patients of other nationalities (non-Tunisian)	52	N/A	12·5 (IQR 20)
Stepien[46]	2017	National Surveillance data	Poland	2003-2015	Malaria cases with mixed invasions	10	N/A	9·5* (SD 9·2) 7·5 (IQR 5-10)

Patient Delay

P. falciparum

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Patient delay (days)
Farnert [55]	2015	retrospective chart review	Sweden	1995-2013	Compares VFR to non VFR's - data combined	501	100	2·5
Roberts [56]	2013	retrospective chart review	UK	2001-2011	Adults >18 years with lab confirmed *falciparum*	773	100	4 (IQR 2-7)
Rossi [57]	2012	retrospective chart review	Switzerland	1999-2007	Adults >16 years with lab confirmed *falciparum*	154	100	3·9*
Vatan [58]	2006	retrospective chart review	France	2001-2002	Lab confirmed *P.falciparum* in adults	107	100	3 (0-98) 9·17*
Parola [59]	2005	prospective observational study	France	2002-2003	Lab confirmed *P. falciparum* in adults >15 years	212	100	4
Askling [60]	2005	Questionnaire	Sweden	1994-2001	Questionnaires sent to patients diagnosed with *P.falciparum*	237	100	2 (0-71)
Miura [61]	2005	retrospective chart review	Japan	1992-2001	Lab confirmed *P.falciparum*	50	100	4·1* (95%CI 2·5-5·7) 2 (IQR 1-5)
Soraa [44]	2006	retrospective chart review	Morocco	2001-2004	Lab confirmed malaria	68	85·3	2
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. falciparum*	14	100	2·4 "average" (0-5)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.falciparum*	1840	100	5·9* (SD 12·5) 3 (IQR 2-6)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.falciparum*	1630	100	8·6* (SD 93·9) 3 (IQR 2-6)
CNRP [15]	2008	National Surveillance data	France	2008	Notified cases of malaria	1885	86	5·6* (SD 0·3) 3 (IQR 2-6)
CNRP [15]	2007	National Surveillance data	France	2007	Notified cases of malaria	1782	86	7·3* (SD 22·6) 3 (IQR 2-6)
CNRP [15]	2006	National Surveillance data	France	2006	Notified cases of malaria	2359	82·6	15·3* (SD 60·7) 4 (IQR 2-9)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. falciparum* cases reported to the CDC	4183	100	5·5* (SD 15·3) 4 (IQR 2-6)

P. falciparum (Severe)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Patient delay (days)
Calvo-Cano [62]	2016	retrospective chart review	Spain	2013-2015	Patients diagnosed with severe malaria	16	100	5 (2·5-11·7)

Santos (a) [63]	2012	retrospective chart review	Portugal	1990-2011	Adults admitted to ICU with severe malaria + survived	50	100	7 (IQR 4-9)
Santos (b) [63]	2012	retrospective chart review	Portugal	1990-2011	Adults admitted to ICU with severe malaria + died	9	100	6 (IQR 4-8)
Gonzalez [48]	2009	retrospective chart review	Spain	1991-2007	Adults admitted to ICU with severe malaria	20	100	4·5 (IQR 3-8·5)
Badiaga [21]	2005	retrospective chart review	France	1996-2002	Patients >15 years admitted with severe malaria (*P.falciparum*)	42	100	3 (0-10)
Marks [64]	2013	retrospective chart review	UK	1994-2010	Adults >18 years with severe malaria admitted to ICU	124	100	4 (IQR 3-6)
McCarthy [18]	2015	retrospective chart review	Canada	2001-2013	Patients with severe malaria	248	94	3 (0-50) 4·2* (SD 5·3)
CDC[17]	2017	National Surveillance data	USA	2003-2014	Severe *P. falciparum* cases reported to the CDC	1075	100	5·6* (SD 9·5) 4 (IQR 2-6)

P. falciparum (Children)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Patient delay (days)
Evans [65]	2014	retrospective chart review	Canada	1997-2013	Lab confirmed *P. falciparum* in children <18 years	76	100	4 (IQR 2-7)
Arnaez [66]	2010	retrospective chart review	Spain	1995-2007	Children aged 14 and under	60	72	4 (0·5-1095)
Ladhani [67]	2010	prospective observational study	UK	2006-2007	Children aged 16 and under	172	86	4 (IQR 2-6)
Dubos [23]	2010	retrospective chart review	France	2000-2006	Children aged 18 and under	120	83	1
Leahy [68]	2009	retrospective chart review	Ireland	1999-2006	malaria cases admitted to children's hospital	67	95	5
Chalumeau [49]	2006	prospective observational study	France	2002	Lab confirmed *P. falciparum* in children <18 years	29	100	3 (0-11) 3·1*
Lanneaux [69]	2016	retrospective case control study	France	2006-2012	Children aged <18 years admitted to ED (controls)	110	100	2 (IQR 1-5)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. falciparum* cases reported to the CDC (aged <18 years)	1089	100	5·7* (SD 10·2) 4 (IQR 2-6)

P. vivax

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.vivax*	Patient delay (days)
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. vivax*	7	100	3·6 "average" (0-9)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.vivax*	117	100	8·6* (SD 29·9) 3 (IQR 2-7)

CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.vivax*	157	100	16·7* (SD 62·3) 3 (IQR 1-9)
Bottieu [28]	2006	retrospective chart review	Belgium	2000-2005	Lab confirmed *P.vivax*	48	100	5 (IQR 3-6)
Parola [59]	2005	prospective observational study	France	2002-2003	Lab confirmed *P. vivax* in adults >15 years	10	100	8·5
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P.vivax* cases reported to the CDC	1161	100	7* (SD 12·7) 4 (IQR 2-8)

P. vivax (Children)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.vivax*	Patient delay (days)
Evans [65]	2014	retrospective chart review	Canada	1997-2013	Lab confirmed *P. vivax* in children <18 years	28	100	6·5 (IQR 3-11·5)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. vivax* cases reported to the CDC (aged <18 years)	184	100	10* (SD 20·3) 5 (IQR 2·5-10)

P. ovale

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.ovale*	Patient delay (days)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.ovale*	97	100	7·7* (SD 18·7) 4 (IQR 2-7)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.ovale*	102	100	9·3* (SD 36·6) 4 (IQR 2-8)
Bottieu [28]	2006	retrospective chart review	Belgium	2000-2005	Lab confirmed *P.ovale*	34	100	5 (IQR 3-7)
Parola [59]	2005	prospective observational study	France	2002-2003	Lab confirmed *P. ovale* in adults >15 years	6	100	3
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P.ovale* cases reported to the CDC	177	100	6·7* (SD 8·6) 4 (IQR 2-7)

P. malariae

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.malariae*	Patient delay (days)
CNRP [15]	2010	National Surveillance data	France	2010	Notified cases of *P.malariae*	45	100	15·6* (SD 21·2) 9 (IQR 3-15)
CNRP [15]	2009	National Surveillance data	France	2009	Notified cases of *P.malariae*	45	100	14·4* (SD 18·5) 9 (IQR 3-17)
Bottieu [28]	2006	retrospective chart review	Belgium	2000-2005	Lab confirmed *P.malariae*	16	100	7 (IQR 4-13)
CDC[17]	2017	National Surveillance data	USA	2003-2014	*P. malariae* cases reported to the CDC	172	100	8·1* (SD 15·3) 4 (IQR 2-9)

Mixed species / Parasite species not reported

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Patient delay (days)
Alaya-Bouafif (a) [54]	2011	National Surveillance data	Tunisia	2002-2007	Notified cases of malaria amongst Tunisian Patients	54	N/A	5 (IQR 6)
Alaya-Bouafif (b) [54]	2011	National Surveillance data	Tunisia	2002-2007	Notified cases of malaria amongst Patients of other nationalities (non-Tunisian)	39	N/A	5 (IQR 3)
Chung [70]	2014	retrospective chart review	Singapore	2000-2010	Adults with smear +ve malaria	214	34 (83)	4 (IQR 3-7)
Miura [61]	2005	retrospective chart review	Japan	1992-2001	Lab confirmed malaria	101	49·5 (50)	4·7* (95% CI 3·7-5·7) 3 (IQR 2-5)

Mixed species / Parasite species not reported (Children)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Patient delay (days)
Parola [59]	2005	Prospective observational study	France	2002-2003	Lab confirmed malaria in children <15 years	42	N/A	2 (0-42)

Medical Diagnostic Delay

P. falciparum

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical diagnostic delay (days)
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. falciparum*	14	100	0·7 days "average" (0-4)

P. falciparum (Severe)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical diagnostic delay (days)
McCarthy [18]	2015	Retrospective chart review	Canada	2001-2013	Patients with severe malaria	248	94	0 (0-864) 30·2* (SD 94·94) (hours)

P. falciparum (Children)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical diagnostic delay (days)
Dubos [23]	2010	retrospective chart review	France	2000-2006	Children aged 18 and under	120	83	0 (IQR 0-1)

Chalumeau [49]	2006	prospective observational study	France	2002	Lab confirmed *P. falciparum* in children <18 years	29	100	0 (0-19) 1·5*

P. vivax

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.vivax*	Medical diagnostic delay (days)
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. vivax*	7	100	4·6 "average" (0-18 range)

Mixed species

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical diagnostic delay
Nakayama (a) [71]	2014	Retrospective report	Japan	1991-2000	Laboratory confirmed cases malaria 1st decade	14	35·7	8·8* (95%CI 5·9-11·7) 7·5 (IQR 5·8-11·8)
Nakayama (b) [71]	2014	Retrospective report	Japan	2001-2010	Laboratory confirmed cases malaria 2nd decade	13	69·2	5·8* (95%CI 3·3 - 8·3) 4 (IQR 3-9)

Treatment delay

P. falciparum

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Treatment delay (days)
Grynberg [72]	2015	retrospective chart review	Israel	2001-2013	Adult Israeli travellers with uncomplicated *P.falciparum*	63	100	4* (SD 6·4)

P. falciparum (Severe)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% (n) *P.falciparum*	Treatment delay (days)
Jaureguiberry (a) [73]	2015	retrospective chart review	France	2011-2013	Patients who received IV artesunate and died	6	100	1·5 (1-5)
Jaureguiberry (b) [73]	2015	retrospective chart review	France	2011-2013	Patients who received IV artesunate and recovered	117	100	4 (2-5)

Medical treatment delay

P. falciparum

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical treatment delay (days)
Askling [60]	2005	Questionnaire	Sweden	1994-2001	Questionnaires (58% response rate) sent to patients diagnosed with *P.falciparum*	237	100	<1 (0-60)
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. falciparum*	14	100	0 "average" (0)

P. falciparum (Severe)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical treatment delay (days)
McCarthy [18]	2015	retrospective chart review	Canada	2001-2013	Patients with severe malaria	248	94	2 (0-864) 29·9* (SD 91·6) (hours)

P. falciparum (Children)

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical treatment delay (days)
Goldfarb [74]	2009	retrospective chart review	Canada	1999-2006	Children treated for malaria after to implementation of protocol	19	95	5·5 (IQR 3-9·25) (hours)

P. vivax

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.vivax*	Medical treatment delay (days)
Higa [14]	2013	Retrospective study	Japan	1998-2012	Laboratory confirmed cases of *P. vivax*	7	100	0·3 "average" (0-1 range)

Mixed species in children

Study author	Year	Study design	Country	Study period	Description of study participants	Sample size	% *P.falciparum*	Medical treatment delay (days)
Maltezou [33]	2013	retrospective chart review	Greece	1972-2012	Children aged 15 and under	22	32	2 (1-4)

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